

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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Applicant(s): STEER et al.

Group Art Unit: 1614

Serial No.: 10/532,039

Examiner: Unassigned

Filed: April 21, 2005  
371(c) Date: September 22, 2005

Docket No.: 110.01980101  
Confirmation No.: 8552



Title: METHODS OF TREATING INJURIES OF THE NERVOUS SYSTEM ASSOCIATED WITH HEMORRHAGE

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

We are transmitting the following documents along with this Transmittal Sheet (which is submitted in triplicate):

- ☒ **Small entity status is entitled to be asserted in the above-identified application.**
- ☒ An itemized return postcard.
- ☐ A Petition for Extension of Time for \_\_ month(s) and a check in the amount of \$\_\_ for the required fee.
- ☒ An Information Disclosure Statement (2 pgs); copy of International Search Report (2 pgs); 1449 forms (19 pgs); and copies of 207 documents cited on the 1449 forms.
- ☐ A request for continued examination (RCE) and a check in the amount of \$\_\_ for the required filing fee.
- ☐ An Appeal Brief and a check in the amount of \$\_\_, for the required Appeal Brief filing fee.
- ☐ A check in the amount of \$\_\_, representing \_\_.
- ☐ A certified copy of a \_\_ application, Serial No. \_\_, filed \_\_\_\_, the right of priority of which is claimed under 35 U.S.C. §119.
- ☐ Other: \_\_.
- ☐ Amendment ☐ No Additional fee is required. ☐ The fee has been calculated as shown:

Fee Calculation for Claims Pending After Amendment					
	Pending Claims after Amendment (1)	Claims Paid for Earlier (2)	Number of Additional Claims (1-2)	Cost per Additional Claim	Additional Fees Required
Total Claims				x \$25 =	
Independent Claims				x \$100 =	
One or More New Multiple Dependent Claims Presented? If Yes, Add \$180 Here →					
Total Additional Claim Fees Required					

**Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 13-4895. Triplicate copies of this sheet are enclosed.**

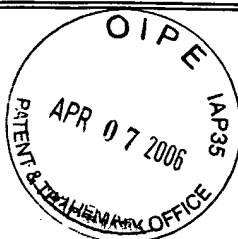
**CERTIFICATE UNDER 37 C.F.R. §1.8:** The undersigned hereby certifies that this Transmittal Letter and the paper(s), as described hereinabove, are being deposited in the United States Postal Service, as first class mail, in a package addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 5 day of April, 2006.

MUETING, RAASCH & GEBHARDT, P.A.  
Customer Number: 26813

By: *Nancy A. Johnson*  
Name: Nancy A. Johnson  
Reg. No.: 47,266  
Direct Dial: 612-305-4723  
Facsimile: 612-305-1228

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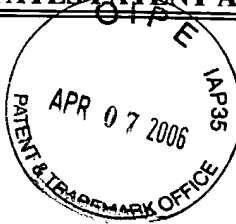
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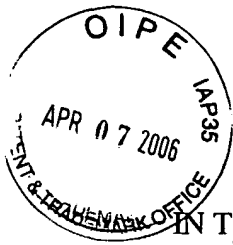
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(SMALL ENTITY TRANSMITTAL UNDER RULE 1.8)



PATENT  
Docket No. 110.01980101

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Serial No.:	10/532,039	)	Examiner:	Unassigned
Confirmation No.:	8552	)		
		)		
Filed:	April 21, 2005	)		
371(c) Date:	September 22, 2005	)		
		)		
For:	METHODS OF TREATING INJURIES OF THE NERVOUS SYSTEM ASSOCIATED WITH HEMORRHAGE			

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In compliance with the duty imposed by 37 C.F.R. § 1.56, and in accordance with C.F.R. §§ 1.97 *et. seq.*, the materials enclosed herewith are brought to the attention of the Examiner as possibly being of interest in connection with the above-identified patent application. Also, enclosed for the Examiner's information is a copy of an International Search Report from related PCT Application No. PCT/US03/31989. Per M.P.E.P. §609, the information cited in the present Information Disclosure Statement shall not be construed to be an admission that the information is, or is considered to be, material to patentability. Consideration of each of the documents listed on the attached 1449 forms is respectfully requested. Pursuant to the provisions of M.P.E.P. §609, Applicants further request that a copy of the 1449 forms, marked as being considered and initialed by the Examiner, be returned with the next Official Communication.

It is believed that no fee is due, as this Information Disclosure Statement is filed prior to the receipt of any Action on the merits. However, in the event a fee is due, please charge any fee or credit any overpayment to Account No. 13-4895.

**Information Disclosure Statement**

Page 2 of 2

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For: METHODS OF TREATING INJURIES OF THE NERVOUS SYSTEM ASSOCIATED WITH HEMORRHAGE

The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if they can be of any assistance during prosecution of the present application.

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Nancy A. Johnson

April 5, 2006  
Date

NAJ/skd

Respectfully submitted

By

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P.O. Box 581415

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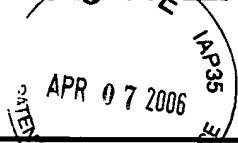
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	Information Disclosure Statement mailed: April 5, 2006	

## U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
	5,656,725	08/12/97	Chittenden et al.			
	5,672,603	09/30/97	Nakai et al.			
	6,544,972 B1	04/08/03	Steer et al.			
	6,555,141 B1	04/29/03	Corson et al.			
	2003 0044413A1	03/06/03	Steer et al.			
	10/549,867	09/22/05	Steer et al.			

## FOREIGN PATENT DOCUMENTS

Examiner Initial	Copy Enclosed	Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	✓	WO 99/15179	04/01/99	PCT				
	✓	WO 2004/043342 A2	05/27/04	PCT				
	✓	WO 2004/096123 A2 & A3	11/11/04	PCT				
	✓	PCT/US06/04394	02/08/06	Steer et al.				

## OTHER DOCUMENTS (Including Authors, Title, Date, Pertinent Papers, etc.)

Examiner Initial	Copy Enclosed	Document Description
	✓	Adjei et al., "Cathepsin B Protease Activity But Not Interleukin 1 $\beta$ -Converting Enzyme (ICE) Proteases Contributes to Camptothecin-Induced Apoptosis in a Human Hepatocellular Carcinoma Cell Line," AASLD Abstract 481, <i>Hepatology</i> , 1996;24(4 Part 2):247A.
	✓	Adjei et al., "Selective Induction of Apoptosis in Hep 3B Cells by Topoisomerase I Inhibitors: Evidence for a Protease-dependent Pathway that Does Not Activate Cysteine Protease P32," <i>J. Clin. Invest.</i> , 1996 Dec;98(11): 2588-2596.

<b>EXAMINER</b>	<b>Date Considered</b>
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	✓	Adjei et al., "Selective Induction of Apoptosis In A Human Hepatocellular Carcinoma (HCC) Cell Line by the Topoisomerase I Inhibitor Camptothecin," Abstract, <i>Gastroenterology</i> , 1996 Apr;110(4):A483.
	✓	Alexander et al., "Aphasia after left hemispheric intracerebral hemorrhage," <i>Neurology</i> , 1980 Nov;30:1193-1202.
	✓	American Heart Association, <i>Heart and Stroke Facts</i> , 1991, Bethesda, MD, pgs. 7-11.
	✓	Auer et al., "Endoscopic surgery versus medical treatment for spontaneous intracerebral hematoma: a randomized study," <i>J. Neurosurg.</i> , 1989;70:530-535.
	✓	Barnaby, "Stroke Intervention," <i>Emerg. Med. Clin. North Amer.</i> , 1990 May; 8(2):267-280.
	✓	Beaufay et al., "Analytical Study of Microsomes and Isolated Subcellular Membranes from Rat Liver I. Biochemical Methods," <i>J. Cell Biol.</i> , 1974;61:188-200.
	✓	Beers et al., Eds., <i>The Merck Manual of Diagnosis and Therapy</i> , 17 <sup>th</sup> Ed., 1999:1452-1476.
	✓	Benedetti et al., "Subcellular changes and apoptosis induced by ethanol in rat liver," <i>J. Hepatology</i> , 1988 Apr;6(2):137-143.
	✓	Benz et al., "Effect of tauroursodeoxycholic acid on bile-acid-induced apoptosis and cytolysis in rat hepatocytes," <i>J. Hepat.</i> , 1998 Jan;28(1):99-106.
	✓	Bernardi, "Modulation of the Mitochondrial Cyclosporin A-sensitive Permeability Transition Pore by the Proton Electrochemical Gradient," <i>J. Biol. Chem.</i> , 1992 May 5;267(13):8834-8839.
	✓	Bogousslavsky et al., "The Lausanne Stroke Registry: Analysis of 1,000 Consecutive Patients With First Stroke," <i>Stroke</i> , 1988 Sep;19(9):1083-1092.
	✓	Boise et al., " <i>bcl-x</i> , a <i>bcl-2</i> -Related Gene That Functions as a Dominant Regulator of Apoptotic Cell Death," <i>Cell</i> , 1993 Aug 27;74(4):597-608.

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	✓	Botla et al., "Ursodeoxycholate Inhibits the Mitochondrial Membrane Permeability Transition (MMPT) Induced by Glycochenodeoxycholate: A Mechanism for Ursodeoxycholate Cytoprotection?" AASLD Abstract 316, <i>Hepatology</i> , 1994;20(4)Part 2:175A.
	✓	Botla et al., "Ursodeoxycholate (UDCA) Inhibits the Mitochondrial Membrane Permeability Transition Induced by Glycochenodeoxycholate: A Mechanism of UDCA Cytoprotection," <i>J. Pharmacol. Exp. Ther.</i> , 1995 Feb;272(2):930-938.
	✓	Bouscarel et al., "Alteration of cAMP-mediated hormonal responsiveness by bile acids in cells of nonhepatic origin," <i>Am. J. Physiol.</i> , 1995 Jun;268(6):G908-G916.
	✓	Bouscarel et al., "Ursodeoxycholic acid inhibits glucagon-induced cAMP formation in hamster hepatocytes: a role for PKC," <i>Am. J. Physiol.</i> , Feb 1995;268(2):G300-G310.
	✓	Broderick et al., "The Risk of Subarachnoid and Intracerebral Hemorrhages in Blacks as Compared with Whites," <i>N. Engl. J. Med.</i> , 1992 Mar 12;326(11):733-736.
	✓	Bullock et al., "Intracerebral Hemorrhage in a Primate Model: Effect on Regional Cerebral Blood Flow," <i>Surg. Neurol.</i> , 1988 Feb;29(2):101-107.
	✓	Calmus et al., "Differential Effects of Chenodeoxycholic and Ursodeoxycholic Acids on Interleukin 1, Interleukin 6 and Tumor Necrosis Factor- $\alpha$ Production by Monocytes," <i>Hepatology</i> , 1992;16(3):719-723.
	✓	Caplan et al., "Intracerebral hemorrhage: An update," <i>Geriatrics</i> , May 1978; 33(5):42-52.
	✓	Caplan et al., "Intracerebral Hemorrhage," <i>Stroke: A Clinical Approach</i> , Stoneham, MA, 1986:261-292.
	✓	Carter et al., "Intracellular hydrogen peroxide and superoxide anion detection in endothelial cells," <i>J. Leukocyte Biol.</i> , 1994 Feb;55(2):253-258.

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	✓	Castro et al., "The Bile Acid Tauroursodeoxycholic Acid Modulates Phosphorylation and Translocation of Bad via Phosphatidylinositol 3-Kinase in Glutamate-Induced Apoptosis of Rat Cortical Neurons," <i>J. Pharm. Exp. Ther.</i> , 2004 Nov;311(2):845-852.
	✓	Cathcart et al., "Detection of Picomole Levels of Hydroperoxides Using a Fluorescent Dichlorofluorescein Assay," <i>Anal. Biochem.</i> , 1983;134:111-116.
	✓	Chazouillères et al., "Ursodeoxycholic acid for primary sclerosing cholangitis," <i>J. Hepatology</i> , 1990 Jul;11(1):120-123.
	✓	Cheng et al., "Caspase Inhibitor Affords Neuroprotection with Delayed Administration in a Rat Model of Neonatal Hypoxic-Ischemic Brain Injury," <i>J. Clin. Invest.</i> , May 1998;101(9):1992-1999.
	✓	Chesney et al., "Collagenase-Induced Intrastriatal Hemorrhage in Rats Results in Long-term Locomotor Deficits," <i>Stroke</i> , 1995 Feb;26(2):312-316.
	✓	Choi, "Ischemia-induced neuronal apoptosis," <i>Curr. Opin. Neurobiol.</i> , 1996 Oct;6(5):667-672.
	✓	Columbano, "Cell Death: Current Difficulties in Discriminating Apoptosis From Necrosis in the Context of Pathological Processes In Vivo," <i>J. Cell. Biochem.</i> , 1995;58:181-190.
	✓	Cooper, "Delayed Traumatic Intracerebral Hemorrhage," <i>Neurosurg. Clin. North Amer.</i> , 1992 Jul;3(3):659-665.
	✓	Datta et al., "Cellular survival: a play in three Akts," <i>Genes Dev.</i> , 1999 Nov 15;13(22):2905-2927.
	✓	De Ryck, "Animal Models of Cerebral Stroke: Pharmacological Protection of Function," <i>Eur. Neurol.</i> , 1990 Feb;30(suppl 2):21-27.
	✓	Desjardins et al., "The Role of Apoptosis in Neurodegenerative Diseases," <i>Metab. Brain Dis.</i> , 1998 Jun;13(2):79-96.
	✓	Dragunow et al., "Apoptosis, Neurotrophic Factors and Neurodegeneration," <i>Rev. Neurosci.</i> , 1998;8(3-4):223-265.

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	✓	Duan et al., "Tauroursodeoxycholic Acid Improves the Survival and Function of Nigral Transplants in a Rat Model of Parkinson's Disease," <i>Cell Transplantation</i> , 2002;11(3):195-205.
	✓	Dupourque et al., "Cytoplasmic and Mitochondrial Malate Dehydrogenases from Beef Kidney," <i>Methods Enzymol.</i> , New York, NY, 1969;13:116-122.
	✓	Dyken et al., "Special Report. Risk Factors in Stroke. A Statement for Physicians by the Subcommittee on Risk Factors and Stroke of the Stroke Council," <i>Stroke</i> , 1984 Nov-Dec;15(6):1105-1111.
	✓	Earnest et al., "Chemoprevention of Azoxymethane-induced Colonic Carcinogenesis by Supplemental Dietary Ursodeoxycholic Acid," <i>Cancer Res.</i> , 1994 Oct 1;54(19):5071-5074.
	✓	Ekshyyan et al., "Apoptosis: A Key in Neurodegenerative Disorders," <i>Curr. Neurovasc. Res.</i> , 2004;1(4):355-371.
	✓	Endres et al., "Attenuation of Delayed Neuronal Death After Mild Focal Ischemia in Mice by Inhibition of the Caspase Family," <i>J. Cereb. Blood Flow Metab.</i> , 1998 Mar;18(3):238-247.
	✓	Fan et al., "Modulation of Retinoblastoma and Retinoblastoma-related Proteins in Regenerating Rat Liver and Primary Hepatocytes," <i>Cell Growth &amp; Differ.</i> , 1995 Nov;6(11):1463-1476.
	✓	Fan et al., "The Retinoblastoma Gene Product Inhibits TGF- $\beta$ 1 Induced Apoptosis in Primary Rat Hepatocytes and Human HuH-7 Hepatoma Cells," <i>Oncogene</i> , 1996 May 2;12(9):1909-1919.
	✓	Fan et al., "The Retinoblastoma Gene Product is a Negative Modulator of the Apoptotic Pathway," <i>Advan. Enzyme Regul.</i> , Tarrytown, NY, 1996;36:283-303.
	✓	Fan et al., "A Novel Link Between REC2, a DNA Recombinase, the Retinoblastoma Protein, and Apoptosis," <i>J. Biol. Chem.</i> , 1997 Aug 1;272(31):19413-19417.
	✓	Fan et al., "Regulation of Apoptosis-Associated Genes in the Regenerating Liver," <i>Semin. Liver Dis.</i> , New York, NY, 1998;18(2):123-140.

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	✓	Fisher, "The Pathological and Clinical Aspects of Thalamic Hemorrhage," <i>Trans. Am. Neurol. Assoc.</i> , Atlantic City, NJ, 1959 Jun 15-17:56-59.
	✓	Fisher, "Clinical Syndromes in Cerebral Arterial Occlusion," <i>Pathogenesis and Treatment of Cerebrovascular Disease</i> , Springfield, IL, 1961:151-181,
	✓	Foulkes et al., "The Stroke Data Bank: Design, Methods and Baseline Characteristics," <i>Stroke</i> , 1988 May;19(5):547-554.
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	✓	Rodrigues et al., "The role of bile acids in the modulation of apoptosis," <i>The Liver in Biology and Disease: Principles of Medical Biology</i> , 2004;15:119-146.
	✓	Rodrigues, et al., "Tauroursodeoxycholic acid, a bile acid with <i>in vivo</i> antiapoptotic and neuroprotective properties," <i>Bile Acid Biology and its Therapeutic Implications</i> , Falk Symposium 141, 2005;192-212.
	✓	Ropper et al., "Cerebral Blood Flow After Experimental Basal Ganglia Hemorrhage," <i>Ann. Neurol.</i> , 1982 Mar;11(3):266-271.
	✓	Rosenberg et al., "Collagenase-Induced Intracerebral Hemorrhage in Rats," <i>Stroke</i> , 1990 May;21(5):801-807.
	✓	Savitz et al., "Apoptosis in Neurological Disease," <i>Neurosurgery</i> , 1998 Mar, 42(3):555-574.
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	✓	Schulze-Osthoff et al., "Cell Nucleus and DNA Fragmentation Are Not Required for Apoptosis," <i>J. Cell Biol.</i> , 1994 Oct;127(1):15-20.
	✓	Schmucker et al., "Hepatic Injury Induced by Bile Salts: Correlation Between Biochemical and Morphological Events," <i>Hepatology</i> , 1990 Nov;12(5):1216-1221.
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	✓	Tapia et al., "Hypertensive Putaminal Hemorrhage Presenting as Pure Motor Hemiparesis," <i>Stroke</i> , 1983 Jul-Aug;14(4):505-506.
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	✓	Walker et al., "Detection of the Initial Stages of DNA Fragmentation in Apoptosis," <i>BioTechniques</i> , 1993 Dec;15(6):1032-1040.
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	✓	Wyllie et al., "Cell Death: The Significance of Apoptosis," <i>Int. Rev. Cytol.</i> , New York, NY, 1980;68:251-306.
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